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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/065,856

11/26/2002

Ann E. Loraine

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02/05/2007

AFFYMETRIX, INC

ATTN: CHIEF IP COUNSEL, LEGAL DEPT.

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SANTA CLARA, CA 95051

EXAMINER

MILLER, MARINA I

ART UNIT

PAPER NUMBER

1631

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

02/05/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

# Office Action Summary

Application No.

10/065,856

Applicant(s)

LORAIN ET AL.

Examiner

Marina Miller

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 30 November 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7, 11-21, 24, 25, 28-37, 40, 41 and 43-45 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |                                                                                                            |                                                                                         |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                           | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

### **DETAILED ACTION**

Applicants' submission filed on 11/30/2006 is acknowledged.

Claims 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 are pending.

Claims 6, 8-10, 22-23, 26-27, 38-39, and 42 are cancelled.

Claims 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 presently are under examination.

Applicants' arguments have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are applied.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Claim Rejections - 35 USC § 112***

#### ***New Matter***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1, as amended, recites "inputting ... probe set identifiers that identify probes on an

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array.” However, “probe set identifiers that identify probes,” does not have support in the specification, claims, or drawings, as originally filed. Applicants point to support in the originally filed disclosure in paragraph [0119] for the claim amendment. The examiner reviewed the specification again, but did not find support for the new limitation. The specification only discloses probe set identifiers that identify microarray probe *sets* [0079]-[0081].

Claims 1, 3, 28, and 43, as amended, recite “fitting probe set identifiers and intensity values to a *plurality* of models.” Applicants point to support in the originally filed disclosure in paragraph [0119] for the claim amendment. However, the examiner reviewed the specification again, but did not find support for the new limitation. The specification only discloses A MODEL (see [0120], also application 60/398,958, which is incorporated by reference, pages 3 and 18).

Claims 1, 3, 28, and 43, as amended, recite specific models of genomic structure (exon structure or location data, protein family classification data, splice variant data, and genomic sequence data). However, specific models of genomic structure do not have support in the specification, claims, or drawings, as originally filed. Applicants point to support in the originally filed disclosure in paragraph [0119] for the claim amendment. The examiner reviewed the specification again, but did not find support for the new limitation. The specification does not disclose a model *of* exon structure or location data, the specification only discloses a model *comprising* data about exon/intron location and/or sequence structure (see application 60/398,958, page 18-19 and figs. 9 and 11). The specification also discloses a model of a particular splice variant and a model of an alternative splice variant that has a known function [0120].

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For the reasons stated above and in the previous office actions, the claims are rejected for reciting new matter.

### ***Enablement***

Claims 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims were rejected in the office actions mailed 10/06/2005 and 6/1/2006 because the specification does not provide guidance for fitting probe set identifiers and intensity values to a model of genomic structure without knowledge of fitting parameters and/or criteria. The specification further does not provide guidance for how to fit (*e.g.*, statistically, physically, *etc.*), what to fit (*i.e.*, it is not known what probe set identifiers and intensity values represent), and what model to fit (*i.e.*, a genomic structure model is not known). The specification also does not provide any disclosure that the recited “fitting” will determine ASVs.

Applicants previously amended the specification, in the response filed 4/6/2006, to introduce the material from application 60/398,958 which is incorporated by reference, disclosing an iterative model fitting, *e.g.*, the Maximum Likelihood method. Applicants further argue that probe set identifiers label probes for reference purposes and are known because they are entered by a user. Applicants further argue that the amended claims recite that “a model genomic structure” is known because the amended claims recite “a model of known genomic

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structure, *such as* exon structure or location data, protein family classification data, splice variant data, and genomic sequence data,” and therefore a genomic model is known.

Applicants’ arguments regarding “how to fit” and what to fit are not persuasive. Although application 60/398,958, incorporated by reference, discloses “how to fit” specific CD44 exon and junction probes and probe hybridization intensities to a simple linear model disclosed in sections “Model Fitting and Minimization” and “Results”, the specification does not disclose how to fit general probe set identifiers (*e.g.*, identified by ID number, even if selected by a user) and unidentified intensities detected by an unknown method (*see* the rejection under 112, second paragraph) to a general model of genomic structure.

Specifically, the specification discloses that probe-set identifiers may encompass a broad class of identifiers (*e.g.*, a name, number, and/or symbol that may be arbitrarily assigned by a manufacturer, pages 32-33), wherein a probe may be almost any molecule (*e.g.*, peptide, nucleic acid, oligosaccharide, oligonucleotide, toxin, venom, epitope, hormone, antibody, *etc.*, [0049]). The claims do not recite any specific probe *set* corresponding to an identifier. Further, intensity is usually represented by a value (*e.g.*, amount of a red or green color, *i.e.*, “20” or “30”). The claims do not recite what the intensity values represent (*e.g.*, binding between two molecules, completion of a reaction, expression, amount of nucleic acids, *etc.*). Further, one does not know what “intensity values” indicate, *e.g.*, whether the higher value represents more (or less) product/binding. Therefore, one has to guess how to fit to a model the probe set identifiers and intensity values, wherein one does not know what the identifiers and values represent (*e.g.*, identifier is ID#345JN and intensity of a red color is 465, wherein the combination of the

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identifier and intensity is not known to be anything in particular). That constitutes undue experimentation.

Further, the specification does not disclose what a model of genomic structure is intended to represent (*e.g.*, a physical model, mathematical model, 3D model, *etc.*). Therefore, a “model of genomic structure” is reasonably interpreted to be a mathematical 3D DNA model. The specification does not provide a disclosure for how to fit intensity values to a “structural” model (*i.e.*, a 3D DNA model) even if it is a mathematical model. Also, the recited model of genomic structure is not limited to comprise “intensity” data, hybridization information, or binding data (or any other type of data “corresponding” to intensity values) that might be compared to the input intensity values. The specification does not provide how to fit the *structural model* to the intensity *values*.

Although the skill of those in the art of mathematical modeling, molecular biology, and bioinformatics is high, one usually compares or “fits” data similar in nature. For example, drug/receptor binding is generally fitted to a corresponding PK/PD model, not to a genomic model; DNA/probe binding data is generally fitted to a genomic structure model. In the latter case, however, one has to know to “what” binding element or probes correspond (*e.g.*, specific alleles, genomic element, *etc.*). One also has to know what intensity values, *per se*, represent (*e.g.*, binding, expression, *etc.*) and the meaning of the relative intensity (*i.e.*, what the increase/decrease of the intensity means). Without knowing anything about what probe sets, probe set identifiers, intensity values, and a model of genomic structure represent, one skilled in the art would not know how to fit intensity *values* to a *model* of general genomic *structure*,

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therefore the claimed method for providing information about biological molecules would require undue experimentation.

For the reasons stated above and in the previous office actions, the examiner maintains the rejection.

*Second Paragraph*

Claims 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, as amended, recites the limitation “inputting ... probe set identifiers that identify probes on an array, and a probe intensity values for each probe.” It is not clear whether “a probe intensity value” is detected because each probe of a probe array comprises, for example, a label, or whether intensity values are those previously generated in hybridization experiments between a probe array and a sample. As the intended limitation is not clear, claims 1-2 are indefinite.

Claim 1, as amended, recites the limitation “inputting ... probe set identifiers and a probe intensity values via a client side interface that is received over an Internet network by a host side.” It is not clear whether identifiers and intensities OR an interface is received by a host side. As the intended limitation is not clear, claims 1-2 are indefinite.

Claims 1, 3, 28, and 43, as amended, recites the limitation “a models of known genomic structure, *such as* exon structure or location data, protein family classification data, splice variant data, and genomic sequence data.” A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered



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indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 1, 3, 28, and 43 recite the broad recitation "models of known genomic structure," and the claim also recites "such as exon structure or location data, protein family classification data, splice variant data, and genomic sequence data," which is the narrower statement of the range/limitation.

It is further unclear whether the claims require a specific model of genomic structure (*e.g.*, exon structure), or a model comprising a combination of data/structures (*e.g.*, exon structure data and splice variant data). It is also unclear whether a *model* of genomic structure OR *genomic structure* IN the model is intended to be the exon structure or location data, protein family classification data, etc. It is further unclear what genomic structure is represented by "protein family classification data," *i.e.*, the relationship between "genomic structure" and "protein family classification data" is not clear. It is also unclear what exon "structure" is intended, *e.g.*, a sequence, 3-D structure, tertiary structure, *etc.* As the intended limitations are not clear, claims 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 are indefinite.

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Claims 1 and 28, as amended, recite the limitation “determining alternative splice variants by ... fitting ... probe set identifiers ... and intensity values to ... models” and further recite “wherein the fit of ... the models to the intensity values indicates the presence of alternative splice variants.” It is not clear what is fitted to a model (and what determines alternative splice variants), *i.e.*, probe set identifiers ... *and* intensity values OR only intensity values. Compare, for example, with claims 3 and 43 reciting “determining alternative splice variants by ... fitting ... probe set identifiers ... and intensity values to ... models” and further reciting “wherein the fit of ... the models to the probe set identifiers and intensity values indicates the presence of alternative splice variants.” As the intended limitation is not clear, claims 1-2, 28-37, and 40-41 are indefinite.

### ***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

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will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-6, M-Thu.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, Ph. D. can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marina Miller  
Examiner  
Art Unit 1631

MM

MARJORIE A. MORAN  
PRIMARY EXAMINER

*Marjorie A. Moran*  
2/1/07